**Ethics of Genetic Testing**

* Definition:
  + A laboratory test of a person’s genes or chromosomes for abnormalities, defects or deficiencies, including carrier status, that are linked to physical or mental disorders or impairments, or that indicate susceptibility to illness, disease or other disorder, whether physical or mental, which test is direct test and not an indirect manifestation of genetic disorders.

**Genetic Testing**

* Two types:
  + Diagnostic
    - Determine cause of a disease
  + Predictive
    - Determine risk for a disorder

**Diagnostic Genetic Testing**

* Even before DNA technology, we have been testing for genetic abnormalities.
  + Sickle cell disease
  + Thallasemia
    - Even though DNA testing is available for these, electrophoresis is more commonly performed.
  + PKU
  + Maple Syrup Urine Disease
    - Since World War II

**Predictive Genetic Testing**

* Analyze chromosomes and patterns of base pairs
* Some examples:
  + Cystic Fibrosis
  + Breast cancer
  + Huntington’s Disease

**Case 1: BRCA-1 (Breast cancer susceptibility gene 1)**

* + Laura is a 38 year old caucasian female who discovers a lump in her breast through self-examination.
  + She has a lumpectomy, and the biopsy shows the tumor to be cancerous.
  + Laura has a strong family history of breast cancer (her mother and grandmother both had mastectomies).
  + She has heard about blood testing to check for the BRCA mutation.
    - **How would you counsel this patient?**
    - **How can the results affect treatment options?**
  + Facts about BRCA-1
    - BRCA-1 and BRCA-2 are tumor suppressor genes.
    - Mutation of these genes is linked to hereditary breast and ovarian cancer.
    - Lifetime risk for breast cancer in general population is 12%.
    - Lifetime risk is 60% for BRCA-1 or BRCA-2.
    - Lifetime risk for ovarian cancer in general population is 1.4%
    - Lifetime risk is 15 - 40% for BRCA-1 or BRCA-2
    - **What do you recommend to Laura?**

**Pros and Cons to Genetic Testing**

* Pros
  + Advance medicine and public health
  + Correlate diseases to genes
  + Allow individuals and families to make lifestyle, fertility and planning decisions.
  + May be reassured by a negative result.
* Cons
  + Payment
    - Almost no insurance companies will pay for out-patient breast cancer testing. ($800)
  + May lose health insurance\*
  + Privacy
    - Your employer/health insurance company has your information
  + Not enough people to offer genetic counseling
  + Is your sense of belonging to an ethnic community  based upon your genes?
* Many argue that these ethical issues must be resolved before it should be done extensively.

**Loss of Health Insurance**

* May 21, 2008, President Bush signed the Nondiscrimination Information Act into law.
  + Prohibits group health insurance plans and issuers of coverage from basing eligibility or adjusting premiums on the basis of genetic information.
  + Ins. companies cannot require or purchase results of genetic tests.
  + Prohibits employers from firing, refusing to hire or otherwise discriminating against (potential) employees.

**Other Concerns**

* + Presymptomatic treatment of patients identified with CF has not been shown to delay onset of disease.
  + Genetically affected children may be discriminated against, by being ‘classified’ by education systems.

**Objections to Genetic Testing**

* It interferes with Mother Nature/God’s will.
* Possibility of “designer embryos”
  + In-vitro-fertilization
    - Remove and test one cell as the embryo starts to  divide
    - Make sure an embryo free of the disease in question is implanted
    - Does this qualify as abortion?
* Slippery slope argument
  + Testing for Down Syndrome and other chromosomal abnormalities may lead, as technology develops, to aborting fetuses disposed to:
    - Violence?
    - Criminality?
    - Low IQ?
    - Homosexuality?
  + Do we want the State to interfere with such decisions, in order to prevent this?

**Case 2: Trisomy 21**

* Carla is a 35 year old female who undergoes routine amniocentesis at 16 weeks gestation
* It is positive for Trisomy 21 (Down Syndrome)
  + **How do you counsel her?**
* Facts about Trisomy 21
  + Impairment of cognitive ability
  + Microgenia and macroglossia, flattened nose
  + Epicanthic fold of eyelid and upslanting palpebral fissures
  + Simian crease in hand
  + VSD, Tetralogy of Fallot
  + Risk of Hirschprung’s Disease, duodenal atresia, imperforate anus, GERD
  + Risk of Alzheimer’s Disease

**Summary**

* Genetic testing may advance medicine and public health by correlating diseases to genes.
* Allow individuals and families to make lifestyle, fertility and planning decisions.
* Payment and privacy issues are problematic.
* Patients may be stigmatized.
* Potential for genetic selection of “ideal” traits.

**Human Embryonic Stem Cell Research (HESC)**

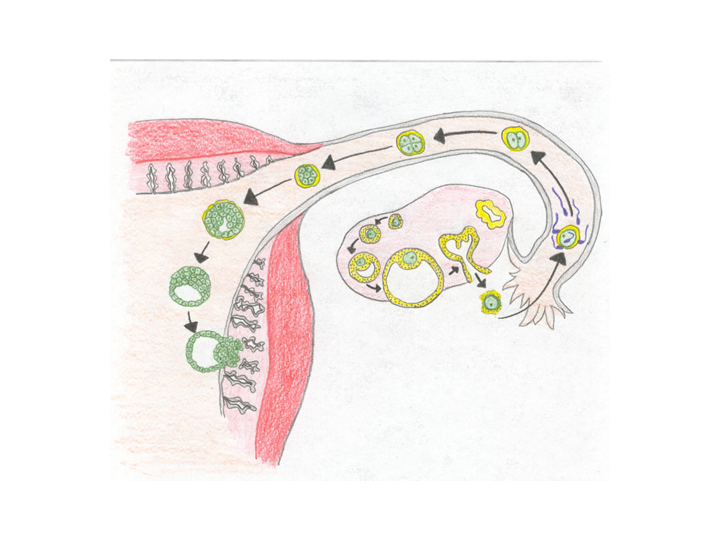
* Stem cells
  + Pluripotent: can differentiate into all cell types of the body
  + Have capacity for self-renewal
* Goal
  + Identify mechanisms that govern cell differentiation
  + Turn HESCs into cell types to treat disease and injury

**Possible Therapies**

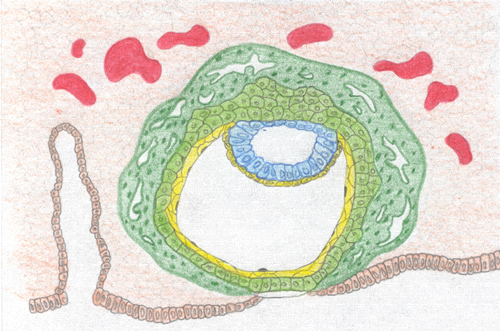
* Somatic Gene Therapy
  + Insertion of a normally functioning gene (via a viral vector) into the nuclei of cultured stem cells.
  + The engineered cells are injected back into the patient where the added gene will restore normal function.
* Germline Gene Therapy (inheritable genetic modification--IGM)
  + Eliminate “bad” genes from the individual and from his descendents
  + Has not yet been attempted on humans
  + Animal examples:
    - GloFish” contain a transgene for a fluorescent protein
    - Transgenic rhesus monkey (ANDi)

**HESCs**

* Derived in vitro at day 5 of embryonic development
* Embryo consists of 200-250 cells
* Most are trophoblast cells
  + Outermost layer of blastocyst
* HESCs are harvested from inner cell mass  of blastocyst
  + 30-34 cells



Inner cell mass

**embryoblast**

**trophoblast**

**Induced Pluripotent Stem Cells (iPSCs)**

* Converting adult human skin cells into cells with the properties of HESCs
* Activate 4 genes in the adult cells to reprogram into pluripotent cells
* Could eliminate need for HESCs
* Unknown if iPSCs have the same potential  as HESCs
* Unknown safety of iPSCs for transplantation in to humans

**Controversies Surrounding HESC Research**

* Is research morally permissible?
  + – Unjust killing of innocent human beings?
* Moral difference between creating embryos for research versus for reproductive ends
* Permissibility of cloning human embryos to harvest HESCs
* Creating human/non-human chimeras

**Argument Against Destroying Human Embryos**

1. It is morally impermissible to kill human beings intentionally.
2. The human embryo is an innocent human being.
3. Therefore it is morally impermissible to kill human embryos intentionally.

* This argument would not suffice to show that most HESC research is impermissible.
* Most investigators engaged in HESC research do not derive the HESCs themselves.
  + They use cell lines that have been provided to them by other researchers.

**Moral Argument Against Using HESCs**

* Must establish complicity in the destruction of embryos.
* To avoid charge of complicity:
  + Those who derived the HESCs would have done so, absent the demand for the cells.

**Other Arguments Against Using HESCs**

* Research with existing HESCs will result in future destruction of the embryos.
* Problem: This criticism is too sweeping.
  + Would affect research with adult stem cells and  non-human animal stem cells.
  + Current HESC research could reduce or eliminate demand for HESCs by enabling the use of alternative sources of cells.
* If it’s wrong to destroy human embryos, even if a researcher does not destroy them, himself, he is morally complicit:
  + He symbolically aligns himself with a wrongful act.
* Problem: There may be a duty to avoid moral taint, but this can be overridden for the sake of a noble cause.

**When does a human being begin to exist?**

* Standard view of those opposed to HESC research:
  + “Genetic” view: you become a human being with the emergence of the one-cell zygote at fertilization
    - Problem: Twinning is possible until days 14-15.
      * Identical (monozygotic) twins are not “identical” people.  An individual who is an identical twin can’t be numerically identical to the one-cell zygote. (Numerical identity must satisfy transitivity)
* “Embryologic” view: you become a human being at gastrulation
  + Some reject that the early human embryo is a human being.
    - Cells that comprise the early embryo are homogeneous.
    - The cells do not function in a coordinated way to regulate and preserve a single life.
    - Each cell is alive, but they only become parts of a human organism around day 16.
    - So, disaggregating the cells at day 5 to derive HESCs does not destroy a human being.
  + But there is some intercellular coordination in the zygote.
    - Some cells become part of the trophoblast and others part of the inner cell mass.
    - Without coordination, all could differentiate in the same direction.
* “Neurological” view: you become a human being when the human EEG pattern is acquired
  + After week 24 of gestation
* Viability view: a fetus should be considered human when it can survive on its own
  + In the past: 28 weeks, lung maturity
  + With advances in technology: 25 week  fetuses survive
    - High risk from physical and/or mental disabilities
  + At birth (when the cord is cut)

**The Morality of Destroying Human Embryos for Research**

* Do human beings have the same moral status at all stages of their lives?
  + Some accept that the human embryo is a human being but does not have the moral status requisite for a right to life.
* Do we appeal to mental capacity?
  + Many people lack such capacity.
* Human infants, the severely mentally retarded, the elderly.
  + Many animals possess such capacity.
    - Chimps and apes

**More arguments...**

* But human infants have the *potential* for developing higher-order mental capacities.
* Maybe infants do not have the intrinsic right to life, but we should treat them as though they do.
* But human *embryos* cannot reason at all, and simply having this potential does not entail that they should have the same status as beings who have already realized this potential.

**When does a human being begin to exist?**

* In“normal”circumstances,50-60%ofallembryos conceived do not survive to birth.
* How much intercellular coordination (or “human function”) must exist to constitute a human organism?
* **This is a *metaphysical* question!**

**What about “doomed embryos”?**

* After fertility treatment, spare embryos are:
  + Stored for future reproductive use
  + Donated to other infertile couples
  + Donated to research
  + Discarded
  + Some argue it is OK to use them in HESC research, once the decision has been made to discard them.

**Arguments for Using “Doomed Embryos”**

* It is morally permissible to kill embryos (at the end of a research project) that were about to be killed by someone else (simply discarded), where killing that individual will help others.
* The decision to discard the embryos causes their death; research just causes the manner of death.

**Arguments Against Using “Doomed Embryos”**

* The decision to discard may have been made as a precondition for donation to research; They may have been inclined to donate to another couple if research had not been available.
* A researcher who receives embryos could choose to rescue them. (But this is illegal.)

**The Ethics of Creating Embryos for HESC Research and Therapy**

* Most HESCs are derived from “left-over” embryos after infertility treatment.
* Problem:
  + These HESCs are not diverse enough to address immune rejection by recipients of stem cell transplants.
  + Researchers need to study particular genetic mutations; this requires cloning technology.

**Moral Distinction of Embryos for Research vs. Reproduction**

* Embryos created for procreation are viewed as a potential child.
* Research embryos are viewed as mere tools.
* But if all research embryos were included in a lottery to be used for reproduction, all would have a chance for developing into mature human beings.  (But they would be viewed as both potential children and as potential research tools.)

**Summary**

* HESC is controversial!
* Some argue that embryos are human beings and should not be killed.
* Others feel that the creation of HESCs for research is justified by the need to make scientific progress to treat disease and injury.
* Many issues are philosophical, rather than scientific or medical.
* Medicine will continue to address these questions, as we make scientific advances.